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FATTY FOODS AND THE RISK OF LUNG CANCER: A CASE-CONTROL STUDY FROM URUGUAY

Eduardo DE STEFANI[1]* Elizabeth T.H. FONTHAM[2], Vivien CHEN[2], Pelayo CORREA[2], Hugo DENEO-PELLEGRINI[1], Alvaro RONCO[1] and Maria MENDILAHARSU[1]

[1]*Registro Nacional de Cancer, Montevideo, Uruguay*
[2]*Section of Epidemiology, Department of Pathology, Louisiana State University Medical Center, LA, USA*

To examine whether fatty-food consumption modifies lung-cancer risk, a case-control study involving 377 patients with lung cancer and 377 controls was conducted in Uruguay. The study was restricted to men. Dietary patterns were assessed in detail using a 64-item food-frequency questionnaire, which allowed the calculation of total energy intake. After adjustment for potential confounders (body-mass index, family history of lung cancer, total energy intake and tobacco smoking), an increase in risk for fatty-food consumption was observed. In particular, fried foods (OR, 1.54; 95% CI, 1.01–2.35), dairy products (OR, 2.85; 95% CI, 1.73–4.69) and desserts (OR, 2.52; 95% CI, 1.54–4.12) were associated with increases in lung-cancer risk and significant dose-response patterns. The association with dairy products was more evident for adenocarcinoma of the lung (OR, 4.18; 95% CI, 1.87–9.36), whereas increased risks for fried-meat and dessert consumption were observed in each cell type. The association with fried-meat consumption was more pronounced for current smokers and for heavy smokers, whereas dairy products and desserts were associated with risk both in current and in past smokers. In conclusion, fat-rich foods and sucrose-rich foods were positively associated with an increased risk of lung cancer. Although the relationship between fat consumption and lung cancer has been reported, the direct association of lung cancer with sucrose-rich foods should be further investigated. *Int. J. Cancer* 71:760–766, 1997.

Wynder *et al.* (1987) showed a strong correlation between fat intake and lung-cancer mortality, based on an ecological study, and suggested that fat could be implicated in lung carcinogenesis. Hinds *et al.* (1983) and Goodman *et al.* (1988) reported increased risks of lung cancer, mainly of the squamous-cell type, associated with high cholesterol intake in 2 case-control studies conducted in the multi-ethnic population of Hawaii; they also found a relationship with total fat and saturated fat. Most, but not all, of the studies dealing with this subject have confirmed these findings. In particular, a positive association was found in 12 studies (Byers *et al.*, 1987; Mettlin, 1989; Jain *et al.*, 1990; Kvale *et al.*, 1983; Shekelle *et al.*, 1991; Fraser *et al.*, 1991; Knekt *et al.*, 1991; Goodman 1992; *et al.*, 1992; Alavanja *et al.*, 1993; Sankaranarayanan *et al.*, 1994; Deneo-Pellegrini *et al.*, 1996; De Stefani *et al.*, 1996), whereas 5 studies failed to find a positive association or were associated with an inverse gradient (Mettlin *et al.*, 1979; Wu *et al.*, 1985, 1994; Heilbrun *et al.*, 1984; Kalandidi *et al.*, 1990).

The present study was designed to determine whether there is increased risk of lung cancer associated with the consumption of fat-rich foods in the Uruguayan diet.

SUBJECTS AND METHODS

Selection of cases

The case series for this hospital-based study in Uruguay comprised all patients with primary lung cancer newly diagnosed in the 4 major hospitals of Montevideo, the capital. Cases included patients from 30 to 89 years of age who had been residents of Uruguay for more than 10 years. Completed questionnaires were obtained from 96% (377 patients) of male lung-cancer patients. Since the incidence rate of lung cancer among females is low (6.7 per 100.000) (Vassallo *et al.*, 1996), these patients were *a priori* excluded from the study because of low accrual. Reasons for not participating were refusal (3%) and terminal illness (1%). Proxy interviews were not included. Cases were interviewed shortly after diagnosis; the mean interval between diagnosis and interview was 25 days (range, 15–45 days). The mean time between the first symptom and diagnosis was 63 days.

Distribution by cell type of the case series is shown in Table I. This distribution closely follows that observed in the population-based cancer registry of Montevideo (Vassallo *et al.*, 1996).

Selection of controls

Hospital controls were frequency-matched to cases by age (10-year group), residence (Montevideo, other counties) and urban/rural status. Controls were admitted for non-neoplastic conditions. Patients with nutritional disorders and diseases related to smoking were ineligible for this study. The most common conditions were traumatic fractures (131 patients, 34.7%), eye disorders (93 patients, 24.7%), abdominal hernia (56 patients, 14.9%) and traumatic injuries (38 patients, 10.1%) (Table II). Controls were identified from the same hospitals as the cases. A similarly high response rate was observed (93%), and reasons for non-response were refusal (5%) and terminal illness (2%). The final number for the control series was also 377 patients.

Questionnaire

Cases and controls were interviewed with a detailed questionnaire, including sections on demographic characteristics; smoking history (age when first smoked, age when ceased smoking, type/color of tobacco, major brands used, life-long average amount in cigarettes per day, duration, duration of hand-rolling, filter-use duration), alcohol consumption (beer, wine and hard liquor in ml ethanol/day), family history of first-degree relatives, height, weight and life-time occupational history, as well as a food-frequency questionnaire with 64 food items. All cases and controls were interviewed in the hospitals.

Food-frequency questionnaire

The dietary questionnaire used in this study included 64 food items plus vitamin and mineral supplements and questions relating to alcoholic beverages, soft drinks, coffee, coffee with milk, tea, tea with milk and "mate". For each food, a commonly used unit or portion size was specified, and participants were asked how often, on average, over the past year, or the year prior to onset of symptoms for the cases, they consumed that amount of each food.

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*Correspondence to: Registro Nacional de Cancer, Avda. Brasil 3080 dep 402, Montevideo, Uruguay. Fax: (598) (2) 42 08 10.

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TABLE I – DISTRIBUTION OF CASES BY CELL TYPE

Cell type	Number	%
Squamous-cell	186	49.3
Small-cell	48	12.7
Adenocarcinoma	88	23.3
Large-cell	12	3.2
Carcinoma NOS	14	3.7
Clinical diagnosis	29	7.7
Total	377	100.0

TABLE II – DISTRIBUTION OF CONTROLS BY DISEASE CATEGORY

ICD-9	Disease	Number	%
800–829	Traumatic fractures	131	34.7
360–379	Eye disorders	93	24.7
550–553	Abdominal hernia	56	14.9
830–959	Trauma	38	10.1
540	Acute appendicitis	17	4.5
710–739	Osteoarticular diseases	16	4.2
454	Varicose veins	14	3.7
680–709	Diseases of the skin	12	3.2
Total		377	100.0

Responses were open-ended, allowing each food to be treated as a continuous variable (Willett, 1990). Responses were recorded in times per day, week or month, the corresponding units being 364, 52 and 12. Responses were converted to times per year, multiplied by the appropriate time units. For example, the intake of a patient who reported drinking a glass of milk 2–3 times per week was recorded as 130 times per year (2.5 multiplied by 52). The authors consider that this method of recording food consumption reflects true consumption more accurately than forcing responses into pre-existing categories.

Statistical analysis

The distribution of all study subjects (cases and controls) was categorized in quartiles (or tertiles in some instances) for each food or food group. Crude and adjusted odds ratios (ORs) were estimated by unconditional logistic regression (Breslow and Day, 1980). Potential confounders were included in the multivariate models. These were age, residence, education, family history of lung cancer, body-mass index, total energy intake and cigarette smoking (in pack-years). We also adjusted for alpha-carotene since this micronutrient was found to be associated with large reduction in risk of lung cancer in a previous analysis of these data and was correlated with fat intake (data not shown). Alternative adjustment for vegetable and fruit intake did not alter our findings.

The test for trend after multivariate adjustment for co-variates was determined by the χ^2 statistic across the vector of indicator variables for the exposure of interest. For all ORs, 95% confidence intervals (95% CI) were calculated. All calculations were performed in the EGRET program (Statistics and Epidemiology Research Corp., 1989).

RESULTS

The distribution of cases and controls by sociodemographic variables, family history of lung cancer in first-degree relatives, body-mass index and tobacco smoking is shown in Table III. Reflecting frequency matching, age, residence and urban/rural status were similar. Cases and controls alike were drawn from a population with low educational attainment and low incomes, but cases were less educated and had lower incomes. These differences were small and not significant. Tobacco smoking was associated with an OR of 16.7 for 81 or more pack-years, and cases had a higher proportion of relatives with a history of lung cancer. There were significant differences between cases and controls in body-mass index: cases were significantly thinner than controls.

TABLE III – DISTRIBUTION OF CASES AND CONTROLS FOR SELECTED VARIABLES[1]

Variable	Cases	Controls	*p* value
Mean age (years)	62.5 (9.4)	62.7 (10.0)	0.74
Mean income (US$)	169.9 (85.8)	165.2 (65.2)	0.44
Mean body-mass index	20.9 (3.4)	21.5 (3.6)	0.06
Residence			
Montevideo	179 (47.5)	179 (47.5)	
Other counties	198 (52.5)	198 (52.5)	1.00
Urban/rural status			
Rural	92 (24.4)	92 (24.4)	1.00
Education (years)			
0–5	222 (58.9)	206 (54.6)	
6+	155 (41.1)	171 (45.4)	0.27
Family history of lung cancer in a first-degree relative			
Yes	33 (8.8)	17 (4.5)	0.02
Tobacco smoking (pack-years)			
Never smokers	23 (6.1)	117 (31.0)	
1–34	40 (10.6)	115 (30.5)	
35–53	87 (23.1)	65 (17.2)	
54–81	111 (29.4)	46 (12.2)	
82+	116 (30.8)	34 (9.0)	<0.001

[1]Standard deviations or percentages in parentheses.

ORs for lung cancer (all cell types plus non-histologically confirmed cases) by quartile (or tertile) of the intake of several fat-rich foods and food groups are shown in Table IV, after adjusting for age, residence, education, family history of lung cancer, body-mass index, tobacco smoking (in pack-years), alpha-carotene and total energy intake. Significant positive trends were seen with increasing consumption of the following food groups: fried meat, dairy products and desserts. Also, individual food items such as whole milk, custard and rice pudding were associated with significantly elevated risks. Red meat, processed meat, white meat and eggs were not associated with the risk of lung cancer.

In Table V, ORs for squamous-cell lung cancer are shown. Red meat, poultry, dairy products and desserts were associated with a monotonic gradient of increased risks. Again, whole milk (OR for the uppermost tertile, 2.62; 95% CI, 1.58–4.34) and rice pudding (OR for the uppermost tertile, 2.44; 95% CI, 1.44–4.14) showed significant positive associations (p value for linear trend <0.001).

ORs for small-cell lung carcinoma are shown in Table VI. Fried meat, desserts and eggs were the only food groups significantly associated with this cell type. The OR for the uppermost tertile of whole-milk ingestion was 2.07 (95% CI, 0.90–4.75), whereas rice-pudding consumption was associated with a significantly elevated OR of 3.01 (95% CI, 1.22–7.39). Custard also was associated with an increased risk for the uppermost tertile of intake (OR, 2.85; 95% CI, 1.20–6.75).

ORs for adenocarcinoma of the lung are shown in Table VII. Again, fried meat, dairy products, milk, desserts and rice pudding were associated with significant dose-response patterns. It should be noted that egg consumption was associated with a 2-fold increase in the risk of adenocarcinoma.

Table VIII shows ORs of lung cancer (all cell types) for major food groups in never/ex-smokers and smokers. Whereas fried-meat intake showed a strong positive association among current smokers, dairy-product and dessert consumption were associated with similar increases in risk in both groups of smokers.

When patients were stratified by pack-years, a significant dose-response for red-meat consumption was observed among heavy smokers (36+ pack/years) (OR for the uppermost quartile, 2.49; 95% CI, 1.16–5.34), whereas no association was observed for the less intense smokers (≤35 pack/years). ORs for dairy-product and dessert consumption were elevated in both groups of smokers (results not shown).

TABLE IV – ODDS RATIOS OF LUNG CANCER ASSOCIATED WITH FATTY-FOOD INTAKE. ALL CELL TYPES[1]

Food	Quartile				*p* value for trend
	1	2	3	4	
Red meat					
OR	1.0	1.24	1.21	1.25	0.41
95% CI	—	0.78–1.97	0.76–1.92	0.78–1.99	
Beef					
OR	1.0	1.08	1.11	—	0.58
95% CI	—	0.70–1.66	0.77–1.61		
Lamb					
OR	1.0	1.08	1.24	—	0.33
95% CI	—	0.73–1.59	0.81–1.89		
Fried meat					
OR	1.0	1.14	1.54	—	0.04
95% CI	—	0.75–1.73	1.01–2.35		
Broiled meat					
OR	1.0	0.84	1.06	—	0.70
95% CI	—	0.55–1.27	0.68–1.64		
Boiled meat					
OR	1.0	1.39	1.18	—	0.53
95% CI	—	0.89–2.15	0.79–1.77		
White meat					
OR	1.0	1.28	1.32	1.22	0.34
95% CI	—	0.82–1.99	0.84–2.10	0.78–1.91	
Poultry					
OR	1.0	1.38	1.21	—	0.29
95% CI	—	0.90–2.11	0.84–1.75		
Fish					
OR	1.0	0.94	1.07	—	0.72
95% CI	—	0.63–1.41	0.71–1.62		
Processed meat					
OR	1.0	0.83	0.90	1.19	0.44
95% CI	—	0.52–1.31	0.57–1.42	0.75–1.89	
Salami					
OR	1.0	0.97	1.45	—	0.08
95% CI	—	0.64–1.45	0.99–2.14		
Sausage					
OR	1.0	1.06	1.05	—	0.79
95% CI	—	0.71–1.59	0.69–1.59		
Ham					
OR	1.0	1.04	1.38	—	0.13
95% CI	—	0.70–1.55	0.93–2.05		
Salted meat					
OR	1.0	0.93	1.19	—	0.65
95% CI	—	0.54–1.62	0.68–2.09		
Total meat					
OR	1.0	1.19	1.28	1.14	0.58
95% CI	—	0.75–1.85	0.79–1.99	0.70–1.79	
Dairy products					
OR	1.0	1.52	1.93	2.85	<0.001
95% CI	—	0.95–2.43	1.20–3.11	1.73–4.69	
Whole milk					
OR	1.0	1.40	2.72	—	<0.001
95% CI	—	0.92–2.14	1.80–4.11		
Cheese					
OR	1.0	1.05	0.92	—	0.69
95% CI	—	0.68–1.61	0.57–1.49		
Butter					
OR	1.0	1.30	1.27	—	0.21
95% CI	—	0.89–1.89	0.83–1.94		
Ice cream					
OR	1.0	1.03	1.09	—	0.74
95% CI	—	0.71–1.49	0.68–1.72		
Desserts					
OR	1.0	1.60	1.90	2.52	<0.001
95% CI	—	0.99–2.58	1.17–3.08	1.54–4.12	
Pie					
OR	1.0	1.10	1.39	—	0.11
95% CI	—	0.74–1.64	0.93–2.10		
Custard					
OR	1.0	1.09	1.68	—	0.02
95% CI	—	0.74–1.61	1.11–2.54		
Rice pudding					
OR	1.0	2.02	3.18	—	<0.001
95% CI	—	1.35–3.02	2.05–4.94		
Eggs					
OR	1.0	0.99	1.04	1.40	0.21
95% CI	—	0.61–1.60	0.66–1.64	0.84–2.31	

[1]Adjusted for age (continuous), residence (Montevideo, other counties), education, family history of lung cancer (yes, no), body-mass index (continuous), alpha-carotene (categorical), tobacco smoking (pack-years, continuous) and total energy intake (continuous).

TABLE V – ODDS RATIOS OF SQUAMOUS-CELL LUNG CANCER ASSOCIATED WITH FATTY-FOOD INTAKE[1]

Food	Quartile				p value for trend
	1	2	3	4	
Red meat					
OR	1.0	1.38	1.30	1.61	0.14
95% CI	—	0.78–2.44	0.74–2.30	0.91–2.83	
Fried meat					
OR	1.0	1.02	1.25	—	0.36
95% CI	—	0.62–1.66	0.80–2.15		
Poultry					
OR	1.0	1.24	1.47	—	0.09
95% CI	—	0.73–2.11	0.95–2.28		
Fish					
OR	1.0	0.82	1.31	—	0.24
95% CI	—	0.50–1.35	0.81–2.14		
Processed meat					
OR	1.0	0.88	0.82	1.17	0.69
95% CI	—	0.51–1.51	0.47–1.43	0.68–2.01	
Dairy products					
OR	1.0	2.01	2.33	2.41	0.005
95% CI	—	1.13–3.58	1.30–4.19	1.30–4.50	
Milk					
OR	1.0	1.89	2.62	—	<0.001
95% CI	—	1.14–3.15	1.58–4.34		
Desserts					
OR	1.0	1.23	1.31	1.81	0.04
95% CI	—	0.70–2.15	0.74–2.33	1.02–3.21	
Rice pudding					
OR	1.0	1.99	2.44	—	<0.001
95% CI	—	1.24–3.23	1.44–4.14		
Eggs					
OR	1.0	0.88	0.98	1.18	0.56
95% CI	—	0.50–1.57	0.58–1.68	0.65–2.13	

[1]Adjusted for age (continuous), residence (Montevideo, other counties), education, family history of lung cancer (yes, no), body-mass index (continuous), alpha-carotene intake (categorical), tobacco smoking (pack-years, continuous) and total energy intake (continuous).

TABLE VI – ODDS RATIOS OF SMALL-CELL LUNG CANCER ASSOCIATED WITH FATTY-FOOD INTAKE[1]

Food	Quartile				p value for trend
	1	2	3	4	
Red meat					
OR	1.0	0.39	0.77	0.99	0.70
95% CI	—	0.12–1.24	0.30–2.01	0.39–2.53	
Fried meat					
OR	1.0	1.43	2.53	—	0.04
95% CI	—	0.55–3.67	1.01–6.33		
Poultry					
OR	1.0	1.31	0.90	—	0.85
95% CI	—	0.54–3.13	0.39–2.05		
Fish					
OR	1.0	1.76	1.49	—	0.40
95% CI	—	0.74–4.19	0.59–3.76		
Processed meat					
OR	1.0	0.84	0.93	0.80	0.73
95% CI	—	0.31–2.25	0.36–2.43	0.29–2.18	
Dairy products					
OR	1.0	0.41	1.49	1.20	0.36
95% CI	—	0.14–1.21	0.59–3.77	0.43–3.34	
Milk					
OR	1.0	0.38	2.07	—	0.12
95% CI	—	0.13–1.13	0.90–4.75		
Desserts					
OR	1.0	2.29	2.70	3.45	0.03
95% CI	—	0.78–6.78	0.88–8.29	1.17–10.2	
Rice pudding					
OR	1.0	1.48	3.01	—	0.01
95% CI	—	0.58–3.74	1.22–7.39		
Eggs					
OR	1.0	1.46	0.66	3.15	0.05
95% CI	—	0.49–4.32	0.21–2.09	1.14–8.69	

[1]Adjusted for age (continuous), residence (Montevideo, other counties), education, family history of *lung cancer (yes, no)*, body-mass index (continuous), alpha-carotene intake (categorical), tobacco smoking (pack-years, continuous) and total energy intake (continuous).

TABLE VII – ODDS RATIOS OF ADENOCARCINOMA OF THE LUNG ASSOCIATED WITH FATTY FOOD INTAKE[1]

Food	Quartile				*p* value for trend
	1	2	3	4	
Red meat					
OR	1.0	2.56	1.63	1.51	0.67
95% CI	—	1.19–5.51	0.74–3.61	0.64–3.56	
Fried meat					
OR	1.0	1.62	2.45	—	0.01
95% CI	—	0.79–3.32	1.19–5.04		
Poultry					
OR	1.0	1.45	0.88	—	0.76
95% CI	—	0.75–2.81	0.47–1.66		
Fish					
OR	1.0	1.70	1.33	—	0.42
95% CI	—	0.89–3.26	0.65–2.70		
Processed meat					
OR	1.0	0.66	1.11	1.66	0.08
95% CI	—	0.29–1.49	0.52–2.34	0.81–3.41	
Dairy products					
OR	1.0	1.34	2.16	4.18	<0.001
95% CI	—	0.61–2.94	0.97–4.82	1.87–9.36	
Milk					
OR	1.0	1.13	3.05	—	<0.001
95% CI	—	0.50–1.35	0.81–2.14		
Desserts					
OR	1.0	2.06	1.97	2.80	0.02
95% CI	—	0.94–4.52	0.89–4.35	1.26–6.22	
Rice pudding					
OR	1.0	2.23	3.54	—	<0.001
95% CI	—	1.14–4.36	1.73–7.25		
Eggs					
OR	1.0	1.23	1.49	1.91	0.10
95% CI	—	0.53–2.84	0.70–3.18	0.84–4.35	

[1]Adjusted for age (continuous), residence (Montevideo, other counties), education, family history of lung cancer (yes, no), body-mass index (continuous), alpha-carotene intake (categorical), tobacco smoking (pack-years, continuous) and total energy intake (continuous).

TABLE VIII – ODDS RATIOS OF LUNG CANCER FOR SELECTED FOOD GROUPS BY SMOKING STATUS, ALL CELL TYPES[1]

Food group	Never/ex-smokers (123 cases)		Current smokers (254 cases)	
	OR	95% CI	OR	95% CI
Red meat	1.0	—	1.0	—
	1.06	0.51–2.22	1.41	0.77–2.58
	1.10	0.51–2.37	1.28	0.71–2.31
	1.16	0.55–2.47	1.32	0.71–2.46
	p for trend 0.69		*p* for trend 0.45	
Fried meat	1.0	—	1.0	—
	0.84	0.42–1.69	1.34	0.78–2.30
	1.20	0.62–2.34	1.92	1.10–3.36
	p for trend 0.51		*p* for trend 0.02	
Dairy products	1.0	—	1.0	—
	1.66	0.71–3.87	1.49	0.83–2.66
	1.85	0.81–4.20	2.13	1.17–3.89
	3.25	1.41–7.47	2.76	1.45–5.27
	p for trend 0.005		*p* for trend <0.001	
Desserts	1.0	—	1.0	—
	1.83	0.79–4.23	1.56	0.86–2.83
	2.48	1.09–5.62	1.69	0.91–3.15
	3.85	1.67–8.89	1.97	1.05–3.69
	p for trend <0.001		*p* for trend 0.04	

[1]Adjusted for age (continuous), residence (Montevideo, other counties), education, family history of lung cancer (yes, no), body-mass index (continuous), tobacco smoking (pack-years, continuous), alpha-carotene (categorical) and total energy intake (continuous).

DISCUSSION

The results of our study provide additional evidence for risk of lung cancer associated with intake of fatty foods such as fried meat, dairy products and desserts, supporting earlier findings (Hinds *et al.*, 1983; Goodman *et al.*, 1988, 1992; Knekt *et al.*, 1991). Of 19 studies investigating the fat/lung-cancer association (Hinds *et al.*, 1983; Goodman *et al.*, 1988, 1992; Mettlin *et al.*, 1979; Wu *et al.*, 1985, 1994; Byers *et al.*, 1987; Mettlin, 1989; Jain *et al.*, 1990; Kvale *et al.*, 1983; Heilbrun *et al.*, 1984; Kalandidi *et al.*, 1990; Shekelle *et al.*, 1991; Fraser *et al.*, 1991; Knekt *et al.*, 1991; Alavanja *et al.*, 1993; Sankaranarayanan *et al.*, 1994; Deneo-Pellegrini *et al.*, 1996; De Stefani *et al.*, 1996), 13 reported positive associations with fat, cholesterol and/or fatty foods (Hinds *et al.*, 1983; Goodman *et al.*, 1988, 1992; Byers *et al.*, 1987; Mettlin, 1989; Jain *et al.*, 1990; Shekelle *et al.*, 1991; Fraser *et al.*, 1991; Knekt *et al.*, 1991; Alavanja *et al.*, 1993; Sankaranarayanan *et al.*, 1994; Deneo-Pellegrini *et al.*, 1996; De Stefani *et al.*, 1996), while 3 reported no association (Heilbrun *et al.*, 1984; Kalandidi *et al.*, 1990; Wu *et al.*, 1994) and 3 reported negative associations, mainly with dairy products and milk (Mettlin *et al.*, 1979; Wu *et al.*, 1985, 1994). It should be noted that several studies focused on the relationship of retinol and lung cancer (Mettlin *et al.*, 1979; Kvale *et al.*, 1983). The 5 cohort studies (Heilbrun *et al.*, 1984; Shekelle *et al.*, 1991; Fraser *et al.*, 1991; Knekt *et al.*, 1991; Wu *et al.*, 1994) provide weaker support for the relationship of fat and lung-cancer risk than do case-control studies: only 3 out of 5 found a positive association with fat or cholesterol consumption (Shekelle *et al.*, 1991; Fraser *et al.*, 1991; Knekt *et al.*, 1991). Discrepancies in the findings of these studies may be due to differences in study design, populations, ranges of intake across populations and dietary-assessment methods (Bostick *et al.*, 1994). The Uruguayan population is characterized by a high intake of meat (beef or lamb), whole milk and sugar-rich foods.

Foods rich in saturated fat and cholesterol promote lung carcinogenesis, according to evidence from studies on experimental animals (Beems and Van Beek, 1984). Laboratory investigations have suggested that cholesterol plays a key role in host immunity; it has also been associated with decreased cell-membrane fluidity

(Cooper and Shattil, 1980). Although the positive association with milk was observed among patients with squamous-cell cancer, it was more evident among adenocarcinoma cases and was also strong among ex/never-smokers, replicating the findings of Alavanja *et al.* (1993). El-Bayoumy *et al.* (1996) have demonstrated that a high-fat diet enhanced DNA methylation in the lung 4 hr after NNK (nitrosonornicotine) treatment in rats.

Although our study was designed to evaluate dietary fat, several of the food groups are potential sources of other carcinogens. For example, fried meat may contain heterocyclic aromatic amines, which have been shown to increase experimental tumors in the breast, colon, kidney and lung of rodents (IARC, 1993), and fried-meat consumption has been suggested as a risk factor for lung cancer by Deneo-Pellegrini *et al.* (1996). Also, desserts are rich in sucrose, which is associated with an increased risk of colorectal cancer (Bostick *et al.*, 1994). Meals rich in sucrose increase a lipemic post-prandial response (Luceri *et al.*, 1996) and enhance hyperinsulinemia, which has been suggested as a risk factor for colon cancer (Giovannucci, 1995). It remains to be determined whether sucrose is a risk factor for lung cancer, after controlling for energy and fat intake.

Strengths of the present study are the sample size, which permitted the analysis of food intake by histologic type, and examination of interactions between fatty-food intake and smoking. As in most case-control studies, recall is a potential bias in the present study. While this possibility cannot be ruled out, it seems unlikely that recall bias alone could fully explain the pronounced association of several food items with lung-cancer risk, taking into account the fact that cases and controls were all hospitalized patients and, consequently, submitted to the same forces of recall. Also, it is unlikely that selective recall for different food items has occurred in each histologic type. Admittedly, patients suffering from lung cancer might be reluctant to admit the extent of cigarette smoking, a well-known cause of lung cancer in the general population, but the relationship between diet and lung cancer has not been publicized in Uruguay. A small sample of cases (38 patients) were re-interviewed. The partial correlation coefficient for milk intake was of 0.65 ($p < 0.001$), whereas smoking intensity in cigarettes/day displayed a coefficient of 0.81 ($p < 0.001$). These data suggest that recall bias for milk consumption and smoking has been minimal. A second common limitation is measurement of usual diet *via* the 1-time administration of a food-frequency questionnaire. Finally, multiple comparisons increase the probability that some results could be due to chance alone.

The use of hospitalized controls as the comparison group has been questioned, on the grounds that such a group may not be representative of the general population and may have illness-related dietary changes. However, appropriately selected hospitalized controls may be the best choice if they are likely to be drawn from the same base population from which the cases were drawn and provide an internally valid comparison (Wacholder *et al.*, 1992). Residual confounding from tobacco smoking is always problematic in lung-cancer studies. After evaluating several indicators of tobacco use, adjustment for pack-years was included in all models. In summary, several high-fat food groups, including dairy products (mainly whole milk), fried meat and desserts, were consistently associated with lung-cancer risk in this study. As stated by Ziegler *et al.* (1996), it is biologically plausible that high-fat foods may be a factor in lung carcinogenesis, a possible mechanism being enhancement of the effect of tobacco.

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APPENDIX – CUT-POINTS FOR MAJOR FOOD GROUPS OR FOOD ITEMS IN SERVINGS PER YEAR

Food group	Percentile				
	25	33	50	66	75
Red meat	178		259		388
Beef		52		104	
Lamb		0		12	
White meat	24		52		102
Poultry		12		48	
Fish		6		30	
Processed meat	79		152		282
Salami		0		18	
Sausage		0		18	
Ham		0		12	
Salted meat		0		18	
Total meat	375		510		719
Fried meat		48		54	
Broiled meat		48		102	
Boiled meat		52		120	
Dairy products	154		481		912
Whole milk		52		547	
Cheese		42		78	
Butter		0		78	
Ice cream		0		12	
Desserts	45		112		206
Pie		0		24	
Custard		0		24	
Rice pudding		3		24	
Eggs	48		102		130